Evaluation of Sentinel Lymph Node Biopsy with Methylene Blue Dye in Early Carcinoma Breast

AHMAD SOHAIL, MUHAMMAD SOHAIL, MUHAMMAD ASIM, JAVED SHAKIR, KHALID M. DURRANI.

ABSTRACT

Aim: To determine the accuracy and feasibility of this procedure to incorporate the sentinel node biopsy in future surgical practice.

Design: Prospective and experimental.

Patients and Methods: Between July 2001 and August 2002, 30 female patients, diagnosed as carcinoma breast on fine needle aspiration cytology with clinical stage T1-2, N0, M0 were recruited for study. Under general anesthesia 1ml 1% methylene blue sterilized dye was injected in subareolar region of breast in all patients and gently massaged the breast for 1-2 minutes to disperse the dye in the lymphatics. Then the blue stained sentinel node was detected and biopsied from the axilla. Later all patients underwent routine mastectomy with axillary clearance.

Results: Over all sentinel node identification rate was 93.4% (28 of 30 patients) and false negative rate was 7.1% (2 of 28 patients). Sensitivity and specificity were (85.7%) and (71.4%) respectively with positive and negative predictive values were (75.0%) and (83.3%) respectively.

Conclusion: The findings of the study support the hypothesis that sentinel node is a true representative and predictor of the axillary nodal status in early carcinoma breast and the procedure can be performed safely with cheaper and feasible methylene blue dye with confidence.

Key words: Sentinel Nodes, Breast Biopsy, Lympho Scintigraphy.

INTRODUCTION

Carcinoma breast is the most common disease of adult females and is the leading cause of the death in their middle age. There is an incidence of 1 in 8 women in United States and 1 in 12 women in England and wales who are expected to get this disease in their life time. Incidence in Pakistan is about 24.4% and due to poor screening program 1/3rd of patients present with locally advanced disease and 17% present with distant metastasis at the time of there initial diagnosis.

Since 19th century Halsted first proposed the importance of lymph nodes, which determine the stage and guide the adjuvant treatment in the carcinoma of breast. In the recent years the surgical treatment of the disease is getting more and more limited from radical mastectomies (Halsted) to the modified radical mastectomy and even the "breast conservation" surgery. The same transformation is now occurring with regard to the axilla where operations evolved from complete axillary node dissection (CAND) to sentinel lymph node (SLN) biopsy might be referred as "axillary conservation". As the incidence of axillary nodal involvement in clinical stage I and II breast cancer is only 4-37% and with the emergence of better adjuvant treatments like chemoradiotherapy and hormonal therapies, there is no survival difference found between immediate removal of nodes or removal later when the nodes are clinically evident. So by doing routine axillary clearance in all those early stage disease, render 63-69% patients to un-necessary axillary dissections. Causes prolonged hospital stay and the complications like numbness, arm odema, brachial plexopathy and seroma formation.

Current methods available to assess the axillary nodal status include clinical, radiological, node sampling and frozen section etc but none of the method has proven its efficacy with full confidence.

Recent studies show that the sentinel lymph node (SLN) biopsy is a newer, reliable and minimally invasive diagnostic method to determine the regional nodal status in breast cancer and provides accurate staging alternative to complete axillary dissection in clinically node negative patients. Sentinel lymph node (SLN) is that first lymph node in the route of the lymphatic channels to the axilla which is infiltrated by the tumour and can predict the status of other nodes in the axillary basin and can be detected by injecting the dye, radioactive material or both into the breast lymphatics.

PATIENTS AND METHODS

This prospective study was conducted at the Department of Surgery, Unit I Shaikh Zayed Federal Postgraduate Medical Institute Lahore from July 2001 to August 2002 after the approval of Hospital Ethical
Committee. A total number of 30 patients were included in the study, all with fine needle aspiration cytology (FNAC) proven carcinoma breast, presented through out patient clinics and were scheduled for modified radical mastectomy. Clinical stage of all pre, peri and post menopausal patients was T1-2, N0, M0 and all were willing for modified radical mastectomy as their surgical treatment. Patients with metastatic, inoperable disease, previous surgery for benign lesions, clinically palpable nodes, larger tumour size or those who were not willing for the procedure were excluded from the study.

At the operation table, prophylactic antibiotics were given at the time of induction to all the patients and after draping 1ml sterilized 1% methylene blue dye was infiltrated with a 23G needle attached to a syringe in the subdermal region of the areola of the diseased breast. Gentle massage of breast done for 1-2 minutes and then with in 5-10 minutes a 3-4cm transverse incision was made just below the hair line in the axilla and by blunt dissection with curved haemostat the blue coloured lymphatic channels were followed which lead to the blue stained node called sentinel lymph node (SLN), the node was identified and carefully dissected out, any other stained node if found in vicinity was also removed.

Following that, in all patients the routine mastectomy with axillary clearance was performed and the harvested node (SLN) and mastectomy with axillary clearance specimen were sent to the histology laboratory fixed in formaline in two separate containers labeled “A” and “B” respectively.

The histology report with thin sliced H & E staining study of both specimen was the end point of the procedure and the results of study were analyzed statistically nominal variables were reported as frequency and percentage numerical data was reported as mean±SD and analysis was performed by utilizing SPSS version 10.

RESULTS

All 30 patients underwent modified radical mastectomy with level II axillary clearance and all primary tumours turned out to be infiltrating ductal carcinomas on histologic examination, mean age of patients was 45±13.48 years with range of (20-70) years and the mean tumour size was 3.7cm with range of (1.5-5cm). Sentinel lymph node (SLN) was detected in 28 out of 30 (93.4%) patients and among those 28 patients total of 32 SLN were detected with mean of 1.14 SLN in each patient. The most frequent location of tumour was upper and outer quadrant 19 of 30 (63.33%).

In 2 of 30 patients the SLN was not detected and the identification rate was 93.4% and among 28 patients with detected SLN, 2 patients who had negative SLN for tumour metastasis showed axillary nodes positive for tumour so false negative rate was (7.1%). Similarly in 4 out of 28 patients (14.2%) the SLN was the only site of metastasis showing the false positive results. Sensitivity and specificity of the method were 85.7% and 71.4% respectively. Similarly the positive and negative predictive values came out to be 75% and 83.33% respectively.

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<td>Identification rate of sentinel lymph nodes.</td>
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DISCUSSION

In the present study the methylene blue dye alone was used for lymphatic mapping and retrieved the identification rate of SLN 93.4% (28 out of 30 patients). Literature reveals identification with blue dye alone in the range of 66-98% and slightly improved rates with combination of both radioactive colloid and blue dye10. In an other study Guenther et al13 has reported 71% identification rate in series of 145 patients using blue dye alone. However in recent studies Edward et al14 and Zerwes et al15 has even shown 100% identification rates.

In the present study we found better results than Giuilliano et al16 Guenther et al and what Kanwal et al17 (83%) has described in the literature. The proposed reasons for lower identification rate in different studies may be the initial experience of the surgeon, high body mass index of patients, the blockage of lymphatics by tumour infiltration or the skip metastasis to other nodes like in level III of axilla, which has 3.5-5% reported incidence in literature18,19.

Lucci et al20 has also described the presence of SLN even in internal mammary chain rather than axilla especially for inner quadrant tumours but has very low incidence.

False negative rate in our study was calculated by dividing the false negative SLN by the total number of patients in which the (SLN) was detected and that came out to be 7.1% which was comparable to the rates reported elsewhere. In the literature the false negative rate varies among surgeons between (0-15)17.

The reason for this variation may be the extensive tumour infiltration causing re-routing of the lymph fluid to the non-sentinel nodes or still the initial experience of the surgeon as the Guillian et al12 in 1994 with 174 patients experience showed (65%) identification and (12%) false negative rates, but later the same group in next series in 199716 published (93%) identification and (0%) false negative rates showing the better understanding of the procedure.
The sensitivity in different series reported in the range of 85-92%22 and the present study revealed 85.7% which was in accordance with the literature. Similarly positive and negative predictive values in literature range from (40-65%) and (88-100%) respectively and our data revealed (75%) and (83.3%) respectively.

The considerable variations in the results are always present in the different series shows the initial experience of the surgeons to learn the procedure and the studies show that this technique has a definite but a short learning curve which can be attained by experience and ultimately achieves more improved identification and lower false -ve rates23.

Moreover it is found that there is no standardization in this procedure so far seen among different surgeons and there is variability in using the dose, materials and choosing the sites for lymphatic mapping, and inspite of the all those methods it does give results. In this study the methylene blue dye was used because it was cheaper, safe, readily available and did not need any hand held gamma camera to detect the radiation. The site of injection peritumoural versus sub-areolar does not make any difference in mapping because breast and the overlying skin, embryologically share the same lymphatics24, however the subareolar route is considered better in case of non palpable and multifocal breast tumours.

CONCLUSION

In this study the use of subareolar methylene blue dye was found cheaper and safe for the sentinel lymph node biopsy and the procedure reliably predicts the axillary lymph node status in early breast cancer, and the findings were comparable with the literature and the procedure can be used with confidence in surgical practice after achieving the short learning curve.

REFERENCES
